

## REMARKS

The following remarks are being submitted as a full and complete response to the Office Action dated December 31, 2008 (U.S. Patent Office Paper No. 20081222). In view of the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, to indicate the allowability of the claims, and to pass this case to issue.

### Status of the Claims

Claims 1-19 stand for consideration in this application, wherein claim 20 is canceled without prejudice or disclaimer. Claims 1 and 8 have been amended to more clearly recite the claimed subject matter. Claims 12 and 17 have been amended to correct minor typographical errors. There is ample written description support for the claim amendments and no new matter is believed to have been added.

### Rejection under 35 U.S.C. § 103(a)

Claims 1-19 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Shimizu et al. (U.S. Patent 5,824,339).

The Examiner contends that the '339 patent discloses coating a core with a drug, preferably a benzimidazole drug, such as lansoprazole or omeprazole, allegedly in combination with crystalline cellulose, wherein the outer layer is an enteric coating to protect acid-sensitive drugs. However, for at least the reasons discussed herein, the '339 patent fails to teach or suggest, or makes obvious every limitation of the claims and withdrawal of the rejection is respectfully requested.

The '339 patent fails to teach, suggest or render obvious the use of microcrystalline cellulose as a stabilizer, and also fails to teach, suggest or render obvious that the benzimidazole compound of formula I is mixed with a stabilizer comprising microcrystalline cellulose. While the '339 patent teaches that the core may include crystalline cellulose, it also teaches that the core need not contain the drug (Column 4, lines 6-33). Thus, the '339 patent actually teaches away from the claimed invention, because it teaches that crystalline cellulose is not required to be mixed with the drug. Even under the more liberal KSR jurisprudence, it is clear that '339 patent provides no motivation to one of ordinary skill in the art to have used microcrystalline cellulose as a stabilizer of the benzimidazole compound of formula I, when in fact the '339 patent teaches that the core comprising crystalline cellulose need not even

contain the drug. For at least the fact that the '339 patent fails to teach microcrystalline cellulose as a stabilizer for benzimidazole compounds, there is no basis for maintaining this grounds for rejection.

The '339 patent also teaches crystalline cellulose as one example of an "additive" from among a long list of very commonly used excipients (Column 6, lines 36-48). However, the '339 patent fails to provide any teaching, suggestion or motivation to specifically select crystalline cellulose for mixture with the benzimidazole compound of formula I. Crystalline cellulose is taught merely as one optional ingredient among a lengthy list of routinely employed excipients, and the '339 patent fails to provide any teaching, suggestion or motivation to specifically utilize microcrystalline cellulose for stabilizing the claimed benzimidazole compound of formula I. The asserted prior art teachings fails to even meet an articulable rationale under the more liberal KSR jurisprudence.

Moreover, in all of the examples of the '339 patent, lansoprazole is combined with the alkaline compound magnesium carbonate. There are no examples in the '339 patent in which microcrystalline cellulose is included for enhancing the stability of a benzimidazole compound of formula I. A person of ordinary skill in the art would clearly have recognized that microcrystalline cellulose is not an alkaline compound, and thus the '339 patent provides no suggestion or motivation to have combined lansoprazole or any other benzimidazole compound of formula I with microcrystalline cellulose.

In addition, as clearly demonstrated in applicants' Declaration under 37 C.F.R. § 1.132 filed herewith, applicants have surprisingly and unexpectedly found that microcrystalline cellulose acts as a stabilizer of the claimed benzimidazole compound of formula I. This surprising and completely unexpected discovery would not have been obvious in view of the '339 patent or in view of any other teachings of the prior art.

There has been a long-felt need in the prior art to achieve stability of such benzimidazole compounds of formula I. The difficulty of providing sufficiently stable pharmaceutical preparations that contain these benzimidazole compounds was well known. Since it was conventionally known that benzimidazole compounds of formula I, in particular omeprazole, are labile in an acidic aqueous solution, benzimidazole compounds were routinely combined in formulations with an alkaline buffer. The many problems inherent to such conventional formulations are discussed, for example, in European patent publication EP-A 0 247 983.

Thus, the finding that microcrystalline cellulose is capable of stabilizing benzimidazole compounds of formula I, in particular omeprazole, pantoprazole, rabeprazole

and lansoprazole, was completely unexpected. The instant inventors unexpectedly observed that when microcrystalline cellulose is used for stabilizing such benzimidazole compounds in a layer of a pellet containing the active ingredient, it is especially advantageous if the microcrystalline cellulose particles are as small as possible in size, and it is presumed that stabilization occurs through interaction with the extensive surfaces of the microcrystalline cellulose. Applicants refer the Examiner to the Table on page 13 of the Specification which shows a comparative analysis of stability of the compounds of the instant invention when stabilized with microcrystalline cellulose versus when stabilized by other means. Not only is superior results evident from the use of microcrystalline cellulose, it came as completely unexpected when conventional teaching favored stabilizing with alkaline compounds.

In view of the failure of the '339 patent to teach nor suggest nor render obvious the claimed invention, and in view of the unexpected stabilizing properties of microcrystalline cellulose, applicants urge the Examiner to withdraw this ground for rejection.

### Conclusion

In view of the foregoing remarks, Applicants submit that there is no basis for applying the previous rejection to the pending claims and withdrawal of the rejection is respectfully requested. The claims are believed to be in condition for allowance, and Applicant earnestly solicits from the Examiner early notification of allowability.

Should the Examiner have any questions or believe a personal or telephonic interview may be in order, she is invited to contact the undersigned at her earliest convenience.

Respectfully submitted,

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